

112. (Amended) A modified signal substance selected from the group consisting of a protein hormone, peptide hormone, growth factor, a haemopoietic growth factor, an inteferon, an interleukin and a colony stimulating factor with enhanced biological activity, antagonistic activity or cell inhibitory activity, wherein said signal substance contains a modification within or in such close proximity to a catalytic center that it effects a biological or chemical feature.

113. (Amended) A modified signal substance being a Zinc binding signal peptide selected from Growth Hormone, prolactin, insulin, and a cytokine acting on the same cytokine receptor superfamily as the IL-3 receptor, said modified substance having been modified in such close proximity to a Zinc binding center that the modified substance has acquired an enhanced biological activity, antagonistic activity or cell inhibitory activity.

119. (Amended) The substance according to claim 118, comprising at least one of the following characteristics

- a) 0.1 ng of the substance, modified IL-3 inhibits up to approximately 50% of 3ng/ml native IL-3;
- b) 3 ng/ml of the substance, modified IL-3 suppresses 80-90% thymidine incorporation of 30-100 ng/ml control IL-3;
- c) the substance modified IL-3 inhibits control IL-3 by a factor of 10-100.

121. (Amended) The substance according to one of claims 112-114, wherein the substance has acquired one of the following combinations of characteristics:

- a) a decreased stability and increased antagonistic activity;
- b) a decreased stability and increased agonistic activity;
- c) an increased stability and antagonistic activity; or
- d) an increased stability in combination with an agonistic activity.

Please add new claims as follows:

of the conditions under which said chemical modification is conducted, said conditions comprising a pH range between a pH of 5.0 and 7.0, time for conducting said modification, and reagent concentrations.

134. (New) The modified signal substance according to claim 113, wherein said cytokine acting on the same cytokine receptor superfamily as the IL-3 receptor is selected from the group consisting of IL-2, IL-3, IL-4, IL-5, IL-6, IL-7, GM-CSF, EPO, and IFN-gamma.

135. (New) The substance according to claim 121, wherein the substance acquiring one of said combinations of characteristics is

- a) acetylated IL-3;
- b) an N-terminally proteased IL-3;
- c) succinylated IL-3; or
- d) a C-terminally proteased IL-3.

136. (New) The method according to claim 108, wherein the chelating is conducted in the presence of urea and EDTA.

See Appendix for changes to claims